UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,438	12/13/2000	Kenneth Churchill Campbell	P31376-C1	5273

1095 7590 07/15/2003

THOMAS HOXIE
NOVARTIS, CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 430/2
EAST HANOVER, NJ 07936-1080

EXAMINER
BERCH, MARK L

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/15/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/735,438	CAMPBELL ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communicati n appears on the cover sheet with th correspondenc address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/117823* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Harnden.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 11-13 rejected under 35 U.S.C. 103(a) as being unpatentable over Harnden.

The reference teaches the relevant compound Famciclovir as compound 14. It exists in two forms, the anhydrate and the monohydrate. The last paragraph on page 1739 clearly states "crystalline monohydrate" in the third sentence, and "this monohydrate" in the fourth sentence. The last sentence of the abstract sets forth the utility. Although the reference does not state whether the anhydrous form or the monohydrate form was used in the clinical trials, the reference places both possibilities in the public domain.

Applicants point out that the elemental analysis was for the anhydrous form. This is not surprising, since the material was crystallized out of a solution of organic solvents. However, the fact is, while Famciclovir is freely soluble in water initially, it immediately forms a hydrate which is sparingly soluble (the indicated paragraph of the reference states 20 mg/mL), so that much of the material will rapidly precipitate out, leaving behind a suspension with some dissolved, and some deposited. Thus, while the originally prepared material, on which the analysis was presumably done, is the anhydrate, the actual aqueous solutions are that of the monohydrate, and the reference recognizes this. Thus, applicants are not seen to have done anything different from the prior art. Applicants dissolved the Famciclovir in water and obtain the crystalline monohydrate, just as the prior art does.

And failing that, it would certainly be obvious to use the monohydrate, since that is what is actually obtained, especially since 14 is designated as a prodrug for "oral administration" --- see last paragraph of the summary section.

The remarks referred to a declaration, but none was actually tendered.

Applicants also refer to comparative data from the specification. This material is not in the form of a proper affidavit. Applicants state "the application contains a declaration from the inventors." It does, but that declaration simply says that they consider themselves to be the first inventors. Declarants are not held to anything they don't actually state. It does not state that the information made of their own knowledge is believed to be true and made with the knowledge that willful false statements are punishable under section 1001 of title 18, etc. Second, the data is not present (e.g. the photographs). Third, there are differences in how the compositions were formulated.

Specifically, the anhydrate compositions have less of both the phosphoric acid di-sodium salt dihydrate (presumably a buffer) and less of the citric acid, and thus it can be reasonably assumed that the two solutions did not have the same acidity (the difference in silicon dioxide is of no relevance). In this regard, the examiner uses the data in the parent; the second column of page 4 in this continuation has nearly all the data in the second column blanked out. In the remarks, applicants present a table of solubility vs. pH for the monohydrate. However, a) this data is not sworn to, b) it doesn't present information for the anhydrate and c) solubility isn't the direct issue here. Applicants also state that the anhydrate form of this phosphoric acid di-sodium salt was used in the anhydrate form of the Famciclovir. However, that is not what is stated in the Table on page 4. It says that the dihydrate was used in both. Fourth, we are given no information on how these suspensions were formed --- what concentrations are they? Fifth, applicants have not explained why this is unexpected, especially in view of the fact that the reference specifically teaches that the anhydrate crystallizes out the monohydrate. Finally, this argument would be relevant only for claims 11 and 15, since those are the only claims limited to the suspensions. Such arguments would be irrelevant for e.g. a regular (albeit dilute) solution.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The purity measure is unclear. Is this purity with regard to things that are not Famciclovir, or purity as compared with the anhydrate? Thus, if the material were 80% monohydrate and 20% anhydrate with nothing else present, would it or would it not meet the claim language?

Claims 7 and 11-13 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for HSV-1, HSV-2 and VZV, does not reasonably provide enablement for Herpes in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The drug Famciclovir (FAMVIR®) is the orally administered prodrug of Penciclovir. These drugs have been extensively studied, been on the market for years (Famciclovir was approved in 1994, Penciclovir in 1996), and have been found to be effective for the treatment of acute herpes zoster (shingles)and of recurrent herpes simplex (genital herpes and cold sores). See the

http://www.nursespdr.com/members/database/ndrhtml/famciclovir.html reference. They have not been made to be effective for any other viruses, despite a few initially promising results. If, as of 2003, these drugs have not been made effective against other viruses, they were certainly not enabled as of 1996. Applicants cite Boyd et al for a result of 52 μg/ml, saying that "Penciclovir is active against CMV" Actually, the reference says more the opposite, with the abstract stating that CMV was "relatively resistant" to the drug. This is not surprising. Penciclovir acts at thymidine kinase, and CMV is generally known not to express this kinase. With regard to Bacon, while it is true that Famciclovir has some fairly modest activity against EBV, no one has ever been able to get the drug to actually work. For example, the most important disease caused by EBV is of course mononucleosis. The skill level in EBV is so low that all attempts to get any antiviral drug to actually work against mononucleosis have proved to be complete failures. As for HHV-8 1) that virus may not have even been isolated at the time of filing, and 2) the Neyts reference which applicants cite is dismissive of this efficacy, saying that neither Penciclovir nor three other drugs "have pronounced anti-HHV-8 activity". In fact, except for that negative teaching, the paper generally ignores Penciclovir. Also, far as the examiner is aware no successful results have been reported for the related Herpes Virus Saimiri (HVS). The previous reference to HVS was correct; the examiner did not intend HSV, which as stated, is enabled. HVS is in the gamma herpes family.

As for prevention, this is clearly not enabled. In fact, the skill level in the prevention art is so low that no antiviral drug has ever been made to be effective in the prevention of any herpes infection. Thus, while FAMVIR® can treat recurrent herpes

sores, it cannot prevent a person from getting a herpes infection in the first place, and it does not prevent a person who is infected from infecting another person.

Specification

The labeling of this case as a Continuation is objected to, as the case was not identical to the parent. Applicants removed almost half of the data from the page 4 table.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.

Mark L. Berch
Primary Examiner
Art Unit 1624

July 11, 2003